

REMARKS

At the outset, applicants would like to thank Examiner Schnizer for his time and consideration of the present application in discussing the application with the undersigned attorney. During the discussion, the issues raised in the outstanding Official Action were discussed.

In the outstanding Official Action, the oath of the inventors was objected to because the specification allegedly contained alterations that were not initialed and/or dated. As noted in the amendment of February 27, 2004, applicants believe that the alterations were a result of a printer error and that the submission of a new oath is not required. As a result, applicants do not believe that an oath or declaration is required. Nevertheless, applicants submit herewith a substitute Declaration and Power of Attorney from the inventors.

Claims 85, 86, 89, 93, 96, 97, 98, 115, and 117 were objected to for allegedly containing several informalities. Applicants believe that the present amendment obviates these objections.

Claim 85 was objected to for reciting the term "Ty9δ2 lymphocytes". The Official Action stated that the term should be made singular. In accordance with the Examiner's suggestion, applicants have amended the claims so that they refer to "a Ty9δ2 lymphocyte".

The Official Action also suggested that the word "and" be inserted after the term "cation" in claims 85 and 96. Accordingly, claims 85 and 96 have been amended to correct this informality.

In claims 88 and 89, the Examiner stated that the word "into" should be substituted for the word "in". As suggested by the Examiner, the word "into" has been substituted for the word "in".

Claim 93 was objected to for misspelling the word "corporal". Claim 93 has been canceled.

Claim 97 was objected to for reciting the term "Ts". However, claim 97 has been amended in a manner so that this term is no longer recited.

Likewise, claims 97 and 115 have been amended so that formula (14) no longer appears in the claims. As a result, applicants believe that the objection to claims 97 and 115 has been obviated by the present amendment.

Claim 98 was objected to for reciting the term "said compound". As suggested by the Examiner, the term has been deleted and the term "said composition" has been inserted.

As to claim 117, applicants have also adopted the suggestion by the Examiner that the term "in" be deleted from the claim.

At this time, applicants would like to thank the Examiner for his suggestions as to how to overcome the objections.

Claims 97-117 were rejected under 35 USC 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants believe that the present amendment obviates this rejection.

Claims 97-115 were alleged to be indefinite because they did not adequately define "R2". The Official Action alleged that the term "a compound allowing the formation of a compound of the formula (14)" was unclear. As discussed with the Examiner, claim 97 has been amended so that this terminology is no longer recited in the claim.

Claims 98, 100-102, and 104 were allegedly indefinite because the claims were drawn to compositions but only recited a single component. The Official Action stated that a composition is considered to be an article of matter that comprises at least two components. As suggested by the Examiner, claims 98, 100-102 and 104 have been amended to recite at least two components.

Claim 101 was allegedly indefinite for reciting the term "a general route". Claim 101 has been amended to recite that the composition is "adapted to be delivered to a primate by a systemic administration". As a result, applicants believe that claim 101 is definite to one of ordinary skill in the art.

The Official Action rejected claims 107-114 for allegedly being indefinite because the claims did not utilize proper Markush language. However, it is believed that claims 107-114 have been amended so that the members of the Markush group have been clearly identified.

Claim 115 was rejected for allegedly being indefinite for reciting a process claim that recited no steps. However, claim 115 has been canceled, the subject matter of which may be pursued in a divisional application.

Claims 116 and 117 were rejected for allegedly being indefinite because nucleosides and phosphoepoxides are not inorganic compounds. Claims 116 and 117 have been amended to recite that the R2 substituent group may be selected from the group consisting of a nucleoside and a phosphoepoxide. The claims do not distinguish between an organic or inorganic substituent. As a result, applicants believe that claims 116 and 117 are definite to one skilled in the art.

Once again, applicants would like to thank the Examiner for his suggestions as to how to overcome these rejections. In view of the above, applicants believe that claims 85-89, 94-99, 101-114, and 116-119 are definite to one skilled in the art.

Claims 97-115 were rejected under 35 USC 112, first paragraph, for allegedly not complying with the written description requirement. Applicants believe that the present amendment obviates this rejection.

In imposing the rejection, the Official Action stated that the claims were drawn to a genus of compounds R2 that allow formation of a compound of structure (14). As a result, the Official Action stated that the claimed genus of compounds was described by functional limitations, not by structural limitations, and that the breadth of the genus was unknown. As a result, the Official Action alleged that claims 97-115 were not supported by the present disclosure.

However, as suggested at page 7 of the Official Action and discussed with the Examiner, R2 has been amended to recite that the substituent group is a "biomolecule". As noted by the Official Action, the specification discloses a wide variety of biomolecules, i.e. nucleic acids, lipids, proteins, and carbohydrates. As a result, the term "biomolecules" is supported by the present disclosure.

Thus, in view of the above, applicants request that the written description rejection be withdrawn.

Claims 85-93, 95, 107-114, and 118 were rejected under 35 USC 112, first paragraph, for allegedly not satisfying the enablement requirement. Applicants believe that the present amendment obviates this objection.

In imposing the rejection, the Official Action stated that while the present disclosure is enabling for methods of activating Ty982 lymphocytes *in vitro*, the present disclosure

does not reasonably provide enablement for activating Ty982 lymphocytes *in vivo*.

At this time, the Examiner's attention is directed to claim 85-93 and 119, which recite methods for activating Ty982 lymphocytes *in vitro*.

However, applicants believe that the present disclosure is enabling for activating Ty982 lymphocytes *in vivo*. At this time, the Examiner's attention is respectfully directed to the present specification at page 21, line 18 to page 22, line 25, wherein one skilled in the art is taught to prepare a composition which can be administered to a primate, and which includes a quantity of a phosphoepoxide compound which (a) is non-toxic and (b) activates Ty982 lymphocytes.

Moreover, Examples 5 to 8 of the application disclose an activation effect of the compounds according to the invention on Ty982 lymphocytes, cultured *in vitro*. The disclosure (see page 21, line 5 - page 23, line 4) provides a transition of these *in vitro* results to an *in vivo* application by teaching one skilled in the art to prepare compositions which can be administered to a primate, to activate its Ty982 lymphocytes, without toxicity.

While the Official Action cites to YAMAGUCHI et al. (1997), JANSSEN et al. (1991) and LOPEZ et al. (2000) as evidence that the claimed compounds cannot activate lymphocytes *in vivo*, YAMAGUCHI et al. (1997), JANSSEN (1991) and LOPEZ et al. (2000)

are not pertinent to the claimed method. These publications are concerned with adoptive immunotherapy.

Adoptive immunotherapy involves an *ex vivo* culture of T cells and their activation by contact with active compounds. Adoptive immunotherapy does not involve directly administering active compounds to the individual to be treated (only activated T cells are (re)introduced into the patient). In adoptive immunotherapy, it is about an *in vitro* use of the active compounds and the amount of activated T cells appears essential for the efficacy of such a treatment.

This stands in contrast to the claimed invention, wherein the claims do not refer to an adoptive immunotherapy method at all, but concern an *in vivo* use of the compounds of the present invention. As claimed and disclosed, these compounds are directly administered to patients with the result that Ty982 lymphocytes are activated *in vivo*. As a result, considerations of the amount of activated T cells, which are generated for adoptive immunotherapy, are not relevant in the present case.

The Official Action also states the method claims are not supported by the present disclosure because the given examples do not prove that the claimed compounds can cure or prevent diseases. However, applicants note that the claims are actually directed to activating Ty982 lymphocytes.

Indeed, applicants believe that the agonist effect of compounds activating Ty952 lymphocytes is only further evidenced by the *in vitro* tests set forth in the present specification.

Thus, as a result, applicants do not believe that the Examiner has met his burden in showing that the claimed invention is not enabled by the present disclosure. Indeed, the Examiner is respectfully reminded that it is a well founded principle that any assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubt so expressed.

As a matter of law, the expressed teaching of the patent specification cannot be controverted by mere speculation and unsupported assertions on the part of the Patent Office. As stated by the Court of Customs and Patent Appeals in the case of *In re Dinh-Nguyen and Stanhagen*, 181 USPQ 46 (CCPA 1974):

Any assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubt so expressed. 181 USPQ at 47.

Such a standard must be applied with great care when the Examiner's conjecture is contrary to the teachings of the specification. As YAMAGUCHI et al. (1997), JANSSEN (1991) and LOPEZ et al. (2000) are not pertinent to the claimed method, applicants believe that the Examiner fails to meet his burden in

APPENDIX:

The Appendix includes the following item(s):

- ☐ - a terminal disclaimer
- ☐ - a 37 CFR 1.132 Declaration
- ☐ - a new or amended Abstract of the Disclosure
- ☐ - a Replacement Sheet for Figure of the drawings
- ☐ - a Substitute Specification and a marked-up copy of the
originally-filed specification
- ☐ - a verified English translation of foreign priority document
- ☒ - a newly-signed oath of the inventors